

Application No.: 09/14,464
Docket No.: BB1193 USDIV

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REMARKS

Reconsideration and allowance are respectfully requested.

Claims 31-43 are now pending, with Claim 31 being the sole independent claim.

Claims 1-30 have been cancelled and Claims 44-66 have been withdrawn without prejudice to or disclaimer of the subject matter recited therein.

Claims 31 and 37-43 have been amended. No new matter has been added.

Turning now to the Office Action mailed November 28, 2003:

Enclosed herewith is a copy of the previously submitted Information Disclosure Statement, the certificate of mailing dated June 15, 2001, and a copy of the postcard date stamped by the U.S. Patent and Trademark Office as being received on June 18, 2001, that were submitted in connection with the above-identified application.

These papers are being resubmitted, since the original papers appear to be missing. Applicants respectfully request entry of these papers with an effective date of June 15, 2001.

Regarding the oath or declaration, Applicants respectfully traverse. Applicants submit that the statutes and rules do not require a date of execution of the declaration. Please see MPEP 802.05 (Oath or Declaration - Date of Execution). See also 35 U.S.C. 115 and 37 CFR 1.63.

Applicants have amended both the title, the abstract and Claim 31 as suggested by the Examiner. Regarding the Section 112, second paragraph rejection, Applicants have amended Claims 37-43 as suggested by the Examiner. No new matter has been added by these amendments. In light of the amendments, withdrawal of these objections/rejections is kindly requested.

Regarding the Section 112, first paragraph enablement rejection, Applicants respectfully traverse.

Applicants submit that the specification enables a person of ordinary skill to make and use the claimed invention commensurate in scope with the pending claims.

Applicants submit that one of ordinary skill would readily recognize where amino acid substitutions could be made to result in a polypeptide sequence having 80% sequence identity to SEQ ID NO:10 while still retaining lysyl-tRNA synthetase activity.

Applicants believe the following three articles to be well-known to one of ordinary skill in the art:

1. Amez et al. (*TIBS* 22:211-216 (1997)), entitled "Structural and functional consideration of the aminoacylation reaction" ("Arnez"; cited in a Supplemental IDS filed simultaneously herewith);
2. Desogus et al. (*Biochem.* 39:8418-8425 (2000)), entitled "Active Site of Lysyl-tRNA Synthetase: Structural Studies of the Adenylation Reaction"

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("Desogus"; cited in a Supplemental IDS filed simultaneously herewith);
and

3. Girtch et al., (*Eur. J. Biochem.* 244:310-317 (1997)), entitled "A root specific iron-regulated gene of tomato encodes a lysyl-tRNA-synthetase-like protein" ("Girtch", cited by the Examiner).

Arnez discusses the common and distinguishing structural and functional themes of the twenty known aminoacyl-tRNA synthetases and lists in Table 1, on page 212, the three conserved motifs for class II tRNA synthetases. Motif 1 contains an absolutely conserved proline, and motifs 2 and 3 contain an invariant arginine. Desogus shows in Figure 5, on page 8424, a partial alignment of selected class II aminoacyl-tRNA synthetases. The invariant arginines and other residues which are important for substrate binding are indicated by asterisks. Girtch shows in Figure 1, on pages 312-313, a complete amino acid sequence of the tomato lysyl-tRNA synthetase with corresponding sequences from other species. The three highly conserved motifs (1, 2 and 3) are underlined.

Appendix A, attached hereto, is a sequence alignment of the following three lysyl-tRNA synthetases:

1. SEQ ID NO:10 of the pending claims (maize lysyl-tRNA synthetase);
2. sequence encoding GenBank Accession Number AF125574; equivalent to NCBI GI 4325324 (*Arabidopsis thaliana* lysyl-tRNA synthetase cited in the instant application); and
3. sequence encoding GenBank Accession Number X94451 (*Lycopersicon esculentum* lysyl-tRNA synthetase cited by the Examiner).

The conserved amino acids among all three sequences can be found in Consensus #1. The three conserved motifs indicative of class II aminoacyl-tRNA synthetases are present and indicated by boxes. The absolutely conserved proline and invariant arginines are present in SEQ ID NO:10 and marked with asterisks.

Attached as Appendix B is a chart setting forth a comparison of the percent identity (and percent divergence in the lower half triangle), using the Clustal alignment method recited in the pending claims, between the three lysyl-tRNA synthetases found in Appendix A.

Applicants submit that there is a well-known correlation between the lysyl-tRNA synthetase activity disclosed and claimed in the instant specification and lysyl-tRNA synthetase protein (and corresponding nucleic acid) structure, based on the remarks above and the conserved structural features.

Given this known correlation between lysyl-tRNA synthetase activity and protein structure, Applicants submit that one of ordinary skill would readily recognize where amino acid substitutions could be made to result in a polypeptide sequence

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having 80% sequence identity to SEQ ID NO:10 while still retaining lysyl-tRNA synthetase activity.

The experimentation necessary to make the claimed invention to the full extent of its scope is not undue in this field, where the level of skill is very high. For example, Applicants disclose methods for expressing the recombinant constructs in monocot, dicot and microbial cells (see Examples 7-9 on pages 22-26). With the expressed polypeptide, activity may be determined using routine tests, such as those presented by Zon et al. (see page 28, lines 4-6 of the instant specification).

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of the claims under 35 USC §112, first paragraph enablement rejection.

Applicants believe that the foregoing is responsive to each of the points recited in the Office Action, and submit that the present application is in allowable form. Favorable consideration and passage to issue are solicited.

Please charge any fees or credit any overpayment of fees which are required in connection herewith to Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company).

Applicants' undersigned may be reached at the below-listed numbers.

Respectfully submitted,

Dawn S. Clark

DAWN S. CLARK, PH.D.
AGENT FOR APPLICANTS
REGISTRATION NO. 42,420
TELEPHONE: 302-695-1080
FACSIMILE: 302-695-3125

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Appendix A

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Consensus #1	SKNA.K.E.K.K.E.....B.....KA.....	D.TQY..NR
BB1193DIVSegIdNo10 GI 4J25324 GenBank X94451	10 20 30 40 50 60 LSLHLRVSPSSPFSRSPHLNEALVSRDN SGLEEK GL TO ON PPAGEGGE 59 E GAADQTTKALSEL MDS9TT NAE SA AG R SSVST 8	
Consensus #1	SKNA.K.E.K.K.E.....B.....KA.....	D.TQY..NR
BB1193DIVSegIdNo10 GI 4J25324 GenBank X94451	70 80 90 100 110 120 Q K E R K L R U E KN - SGKP S V EEE A 118 Q K Q M Q K R D AE KQP ASS V EEE A 94 R K K A E Q L -- QEK A V RQMEQHNLPEN L A 61	
Consensus #1	G.NPYPHKF...S.P..T..Y..L..G.....	LAGR...KR.SSS
BB1193DIVSegIdNo10 GI 4J25324 GenBank X94451	130 140 150 160 170 180 A D T V P G I V K RT SE KLT VA C N T 178 Y A E K E A S K T G S N D H V N A S T 154 R N I E R E S T F I T F S R A H T F P V I D M 121	

Appendix A

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motif 1

Appendix A

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		motif 2									
		N.L...L..R..PELYLK.L.VGG	.RVYE.GK.FRNQG.DLPR.PET.CE.YMA.ADY								
Consensus #1		370	380	390	400	410	420				
BB1193DIVSeqIdNo10		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
GI 4325324		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
GenBank X94451		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
Consensus #1		430	440	450	460	470	480				
BB1193DIVSeqIdNo10		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
GI 4325324		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
GenBank X94451		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
Consensus #1		490	500	510	520	530	540				
BB1193DIVSeqIdNo10		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
GI 4325324		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				
GenBank X94451		[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]				

Appendix A

Consensus #1	SPLAK..RS..GLTERF*	L.F.	N..*	E..C.	AYTELNDP..QR..RF..QLKDRQ..GDDAW..L
	550	560	570	580	590
BB1193DIVSeqIdNo10 GI 4325324 GenBank X94451	R S K S R E	V I R R D	E D T A E	E D T A E	586 563 541
Consensus #1	DE..F..ALEYGGL.PTGG.G.GIDRL.MLLTDS.N.REV..FPAN..	610	620	630	640
BB1193DIVSeqIdNo10 GI 4325324 GenBank X94451	N I P L M	S L F V I	K F P Q E	K F P Q E	634 623 588
Consensus #1	motif 3				
BB1193DIVSeqIdNo10 GI 4325324 GenBank X94451					634 626 588

Consensus #1: When all match the residue on the Consensus show the residue of the Consensus, otherwise show '*'
 Shaded (with black at 40% fill) residues that match the Consensus named "Consensus #1" exactly.

The three highly conserved motifs (1, 2 and 3) are indicated by boxes. Residues which are important for substrate binding are indicated by asterisks.

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Appendix B

Percent Identity

	1	2	3	
1	■	67.7	64.5	1
2	36.0	■	60.2	2
3	43.4	50.1	■	3
	1	2	3	

Divergence